Dosage of Single Low-Dose Primaquine to Stop Malaria Transmission

To The Editor—The World Health Organization (WHO) recommends the use of single low-dose primaquine (SLD-PQ) to reduce *Plasmodium falciparum* malaria transmission [1]. Chen et al assessed the safety of 0.40 and 0.50 mg/kg SLD-PQ usage in glucose-6-phosphate dehydrogenase (G6PD)-deficient adult males in Mali, providing evidence that extending the upper bound of the therapeutic dose range of SLD-PQ is possible [2]. The Dominican Republic (DR) is now (2016–2020) under a strategic plan towards malaria elimination (a joint effort between Pan American Health Organization and the United Nations Millennium Development Goals); it is still considered a malaria endemic country with the highest risk in its far western region. DR is one of the few countries in the world where chloroquine is the recommended first-line treatment for uncomplicated *P. falciparum* malaria, administered together with SLD-PQ in a 0.75-mg/kg regimen, with no alarming secondary effects reported or known to occur due to this regimen [3].

Because the DR population has a strong African ancestry influence [4], a high incidence of G6PD deficiency is expected to occur. We evaluated the *G6PD A*− allele (containing the pathogenic G202A substitution), classified as WHO class III variant [5] and most prevalent in Africans [6], in 343 febrile patients from DR. Samples were collected at the Jaime Mota Regional Hospital in Barahona (246), the Vinicio Calventi Hospital (6) and Robert Reid Cabral Hospital (2) in Santo Domingo, and the San José de Ocoa Hospital (1), as well as in primary health care centers in Barahona (73), Dajabón (6), Santo Domingo (5), La Altagracia (2), Bahoruco (1), and La Vega (1) provinces. Samples were collected between 2011 and 2016 with informed consent and as approved by the DR institutions: Universidad Autónoma de Santo Domingo, Research Council of Faculty of Sciences, the National Health Research Department of the Ministry of Health and the Institute of Microbiology and Parasitology (IMPA) Bioethics Committee. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1964, amended in 2008.

DNA was extracted from filter papers (104) and also from collected Rapid Diagnostic Test Cards (239) (First Response Malaria Ag. *P. falciparum* (HRP2) Card Test, Premier Medical Corporation Ltd.) using NYZ Blood gDNA Isolation Kit (NZYTech). The reactions were run into a Biorad CFX96 Touch Real-Time PCR Detection System using a commercial TaqMan single nucleotide polymorphism (SNP) genotyping assay (SNP ID: rs1050828; Applied Biosystems).

Results showed that the *G6PD A*− allele is present in 20.7% of the population (71 samples) with 20 (5.8%) of Dominicans being male hemizygous or female homozygous and 51 (14.9%) of female Dominicans being heterozygous, correlating with frequencies observed in African populations [6].

Taken altogether, the experience in DR using SLD-PQ support the extension of the upper bound of the therapeutic dose range of SLD-PQ with successful clinical results.

Notes

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References

1. World Health Organization. WHO policy brief on single-dose primaquine as gametocytocide in *Plasmodium falciparum* malaria January 2015. Geneva: WHO, **2015**.
2. Chen I, Diawara H, Mahamar A, et al. Safety of single dose primaquine in

G6PD-deficient and G6PD-normal males in Mali without malaria: an open-label, phase 1, dose-adjustment trial. J Infect Dis **2018**; jiy014.
3. Montero JMP. Guía para el diagnóstico, manejo y prevención de la malaria. Santo Domingo, Dominican Republic: Ministerio de Salud Pública y Asistencia Social, Centro Nacional de Control de Enfermedades Tropicales, **2011**.
4. Institute for Cultural Diplomacy. Introduction to the African diaspora across the world. http://www.culturaldiplomacy.org/index.php?en_programs_diaspora. Accessed 17 January 2018.
5. World Health Organization. Glucose-6-phosphate dehydrogenase deficiency. WHO Working Group. Bull World Health Organ **1989**; 67:601–11.
6. McDonagh EM, Thorn CF, Bautista JM, Youngster I, Altman RB, Klein TE. PharmGKB summary: very important pharmacogene information for G6PD. Pharmacogenet Genomics **2012**; 22:219–28.

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